

REMARKS

Claims 1-11 and 14-23 are pending in the present application. Claims 14-17 have been withdrawn from consideration by the Examiner. Claims 1, 2, 6-8, 10, and 18-23 have been amended. Support for the amendments can be found throughout the specification, for example, in the examples. No new matter has been added. After reconsideration of the rejections of record, claims 1-11 and 14-23 will be pending in this application.

I. Restriction and Election of Species Requirement

The Office has required restriction between one of two Groups, as shown below:

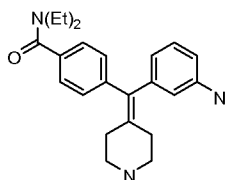
Group I, claim(s) 1-11 and 18-23, drawn to compounds and processes of preparing these compounds; and

Group II, claim(s) 14-17, drawn to the uses of the compounds.

Pursuant to a telephone conference held with the Examiner on May 8, 2007, Applicants elected Group I with traverse, and hereby affirm this election. Applicants further provisionally elect N,N-diethyl-4-[{3-[(phenylacetyl)amino]phenyl}(piperidin-4-ylidene)methyl]benzamide with traverse (Compound 18, page 51, lines 10-11). The claims readable on the elected species, including any claims subsequently added are as follows: claims 1, 8-11, and 21 of Group I and claims 14-17 of Group II. The Office alleges that the “inventions listed as Groups I-II do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical feature” (Office Action, page 2). The Office further alleges that “Group I and II are linked by the technical feature of formula I”, but, “as evidenced by WO 9828275, [a] compound of formula I does not make a contribution over the prior art and does not link the product and method claims into a single general inventive concept” (Office Action, page 2).

Applicants, however, respectfully assert that the compounds of Formula I of the present application are not obvious over WO 98/28275 for the reasons summarized in section V of this response. As the claimed compounds of Formula I are non-obvious, the technical feature of Formula I does make a contribution over the prior art and can link the product and method claims into a single inventive concept. Accordingly, Applicants respectfully assert that Groups I and II relate to a single general inventive concept and request that the restriction requirement be withdrawn.

Additionally, Applicants respectfully traverse the election of species requirement. As will be appreciated, when the members of a Markush group are “so closely related that a search and examination of the entire claim can be made without serious burden, the examiner must examine all the members of the Markush group in the claim on the merits, even though they may be directed to independent and distinct inventions.” MPEP § 803.02. In such a case, it is inappropriate for the examiner to require a provisional election of a single species. MPEP § 803.02. The compounds of Group I can be searched in a single query as they share the following



moiety: . Accordingly, Applicants respectfully assert that all of the compounds of Group I can be searched and examined without serious burden on the Office and request that the election of species requirement be withdrawn.

II. Nonstatutory Obviousness-Type Double Patenting Rejection

Claims 1-2 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting over claims 1-4 and 8 of copending U.S. Patent Publ. No. 2007/0099957 (hereinafter “the ‘957 publication”), and claim 11 is provisionally rejected on the ground of nonstatutory obviousness-type double patenting over claim 5 of the ‘957 publication. Claims 1-2 and 11 are also rejected on the ground of nonstatutory obviousness-type double patenting over claims 1-4 and 8 of U.S. Patent Appl. No. 10/555,980 (hereinafter “the ‘980 application”). As a preliminary matter, Applicants respectfully notes that the ‘980 application and the ‘957 publication are the same application. For the sake of clarity, Applicants will refer to the ‘957 publication throughout this section of the response.

Applicants respectfully note that the present application is a § 371 application of PCT Appl. No. PCT/SE2003/001705 filed Nov. 5, 2003, while the ‘957 publication is a § 371 application of PCT Appl. No. PCT/GB2004/002074 filed May 13, 2004. As such, the present application is the earlier filed of the two applications. Applicants respectfully assert that when a "provisional" nonstatutory obviousness-type double patenting (ODP) rejection is the only rejection remaining in the earlier filed of two pending applications, the Office should withdraw the obviousness-type double patenting rejection in the earlier filed case and permit it to issue as a

patent without requiring a terminal disclaimer. As a result, Applicants will await a notice of allowable subject matter in the application at issue before responding further.

III. Claim Rejections under 35 U.S.C. of § 112, second paragraph

Claims 1-10 and 18-23 are rejected under 35 U.S.C. of § 112, second paragraph, as allegedly indefinite for failing to point out and distinctly claim the subject matter which applicant regards as the invention. In particular, the Office objects to the phrase “diastereomers, enantiomers, or mixtures thereof” in the claims. As this term does not appear in the claims, Applicants respectfully request that the claim rejections under 35 U.S.C. of § 112, second paragraph, be withdrawn.

IV. Claim Rejections under 35 U.S.C. of § 112, first paragraph

Claims 1-10 and 8-23 are rejected under 35 U.S.C. § 112, first paragraph, as allegedly lacking enablement. While conceding that the claims are enabled for compounds of formula I having particular values for R^1 , R^2 , and R^3 , the Office alleges that the specification does not enable one skilled in the art to use the compounds of Formula I having values for R^1 , R^2 , and R^3 that are different those listed on page 9 of the Office Action without undue experimentation. The Office alleges that there is no reasonable basis that the “myriad of compounds embraced by the present formula (I) will all share the same biological properties”, in light of the breadth of the claims, the unpredictability of the pharmaceutical arts, and the working examples (Office Action, pages 10-12). For example, the Office states that Applicants’ specification only contains a statement of an intent to make and use the claimed compounds the Office asserts are not enabled, and describes only working examples encompassing compounds with particular radicals as specified on page 9 of the Office Action.

As will be recognized, the enablement requirement of § 112 is satisfied so long as a disclosure contains sufficient information that persons of ordinary skill in the art having the disclosure before them would be able to make and use the invention. *In re Wands*, 8 U.S.P.Q.2d 1400 (Fed. Cir. 1988) (the legal standard for enablement under §112 is whether one skilled in the art would be able to practice the invention without undue experimentation). In this respect, the following statement from *In re Marzocchi*, is noteworthy:

As a matter of Patent Office practice, then, a specification

disclosure which contains a teaching of the manner and process of making and using the invention in terms which correspond in scope to those used in describing and defining the subject matter sought to be patented **must** be taken as in compliance with the enabling requirement of the first paragraph of § 112 unless there is reason to doubt the objective truth of the statements contained therein which must be relied on for enabling support. Assuming that sufficient reason for such doubt does exist, a rejection for failure to teach how to make and/or use will be proper on that basis; such a rejection can be overcome by suitable proofs indicating that the teaching contained in the specification is truly enabling.

... it is incumbent upon the Patent Office, whenever a rejection on this basis is made, to explain why it doubts the truth or accuracy of any statement in a supporting disclosure and to back up assertions of its own with acceptable evidence or reasoning which is inconsistent with the contested statement.

169 U.S.P.Q. 367, 369-370 (C.C.P.A. 1971) (emphasis added). Thus, any assertion by the Patent Office that an enabling disclosure is not commensurate in scope with the protection sought must be supported by evidence or reasoning substantiating the doubts so expressed. *In re Dinh-Nguyen*, 181 U.S.P.Q. 46 (C.C.P.A. 1974); *In re Bowen*, 181 U.S.P.Q. 48 (C.C.P.A. 1974).

Applicants maintain that while undue experimentation would not be required to practice the entire scope of the invention as originally filed, in order to expedite prosecution, Applicants have amended claims 1, 2, 6-8, 10, and 18-23 to more closely conform the definition of R³ to the exemplified compounds. Applicants respectfully assert that the specification of the present application enables one of ordinary skill in the art to use the claimed invention, as amended, without undue experimentation. For the Office's convenience, Applicants submit Appendix A herewith to show that a working example supports each base group within the definition of R² and R⁸ and nearly every base group in R¹. Applicants also respectfully direct the Office's attention to page 31, lines 16-21 of the specification, wherein at least some of the compounds of the presently claimed invention are stated to exhibit binding affinity (IC₅₀) and human δ -opioid receptor activity (EC₅₀ and % E_{max}) within specifically identified ranges. As will be appreciated, Applicants "are not required to disclose every species encompassed by their claims even in an **unpredictable** art" for a generic claim to be fully enabled. *In re Angstadt*, 537 F.2d 498, 502 (C.C.P.A. 1976) (emphasis added) (finding a generic claim enabled where the specification

disclosed 40 examples). In light of the direction provided by the 53 working examples and the data in the specification, and the fact that Applicants' specification discloses an example falling into nearly all of the presently claimed R¹, R², and R³ moieties. Applicants' respectfully assert that the full scope of the presently claimed invention is enabled. Accordingly Applicants respectfully request the Office to withdraw this rejection.

V. Claim Rejections under 35 U.S.C. § 103

Claims 1-10 are rejected under 35 U.S.C. § 103 as allegedly obvious over PCT Publ. No. WO98/28275 (hereinafter "Delorme"). In order to establish a prima facie case of obviousness, the Office has the burden of showing the following three criteria: 1) a suggestion or motivation to modify or combine the reference teachings; 2) a reasonable expectation of success; and 3) the teaching of all the claim limitations by the reference(s). MPEP § 2143.

Applicants respectfully assert that Delorme does not teach or suggest the compounds of claim 1. Delorme discloses a large genus of compounds of Formula I having a large number of values for A, B, R¹, R², and R³. By contrast, claim 1 of the present application recites a group of compounds having particular values at each position of the (piperidin-4-yl)idene moiety. In particular, the compounds of claim 1 of the present application have a **substituted** amino group at the *meta* position of one of the phenyl rings, where R¹ cannot be hydrogen. One of ordinary skill in the art would not be motivated to choose this particular substituted phenyl ring out of the multitude of variables disclosed for the A and B rings, particularly in combination with the other variables recited by claim 1 of the present application. While the compound in Example 41 disclosed in Delorme has an amino group on one phenyl ring, Delorme's Example 41 amino group—unlike the amino group of the presently claimed invention—is unsubstituted (Delorme, page 69). Indeed, Delorme does not provide any suggestion that would have motivated one of ordinary skill in the art to replace one of the Delorme Example 41 amino group hydrogens, let alone suggest even one of presently claimed R¹ groups as possible replacements therefor. Further, the Federal Circuit has made it clear that a claimed compound is not obvious over a prior art compound unless there is "a preliminary finding that one of ordinary skill in the art would have selected [the prior art compound]...as a lead compound." *Takeda Chemical Industries, Ltd. v. Alphapharm Pty, Ltd.*, 492 F.3d 1350, 1357 (Fed. Cir. 2007) (finding a claimed compound non-obvious because one of ordinary skill in the art would not have selected

the prior art compound as the lead compound out of the “hundreds of millions” of compounds disclosed by the prior art patent). As Delorme fails to provide any motivation that would have led one of ordinary skill in the art to choose the compound of Example 41 as a lead compound out of the many compounds covered by the generic formula therein, Applicants respectfully assert that claims 1-10 are not obvious over Delorme. Accordingly, Applicants respectfully request the Office to withdraw this rejection.

VI. Conclusion

Applicants respectfully submit that the claims are in condition for allowance. An early notice of the same is earnestly solicited. The Examiner is invited to contact Applicants’ undersigned representative at (610) 640-7854 to resolve any remaining issues.

The Commissioner is hereby authorized to debit any underpayment of fee due or credit any overpayment to Deposit Account No. 50-0436.

Respectfully submitted,

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Appendix A

Variable	Examples
R¹	
C ₃₋₆ alkyl	12
C ₆₋₁₀ aryl	35, 36, 37
C ₂₋₉ heteroaryl	
C ₆₋₁₀ aryl-C ₁₋₄ alkyl	1, 4, 5, 6, 7, 8, 38, 39, 42
C ₂₋₉ heteroaryl-C ₁₋₄ alkyl	2, 3, 9, 10
C ₃₋₁₀ cycloalkyl	13, 14, 15, 16, 43
C ₃₋₁₀ cycloalkyl-C ₁₋₄ alkyl	11, 40, 41
R ⁸ -C(=O)-	17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 46, 47, 48, 49, 50, 51, 52, 53
R ⁸ -S(=O) ₂ -	33, 34
R ⁸ -S(=O)-	
R ⁸ -NH-C(=O)-	30, 31, 54
R ⁸ -C(=S)-	
R ⁸ -NH-C(=S)	
R⁸	
C ₃₋₆ alkyl	46
C ₆₋₁₀ aryl	17, 29, 30, 33, 49, 51, 53, 54
C ₂₋₉ heteroaryl	47, 48, 50, 52
C ₆₋₁₀ aryl-C ₁₋₄ alkyl	18, 21, 22, 25, 26, 27, 28, 31, 34
C ₂₋₉ heteroaryl-C ₁₋₄ alkyl	23, 24
C ₃₋₁₀ cycloalkyl	19
C ₃₋₁₀ cycloalkyl-C ₁₋₄ alkyl	20
R¹ and R²	
C ₁₋₃ alkylene, which form a ring	44, 45
R²	
H	1-15, 17-28, 30-35, 38-42
C ₁₋₆ alkyl	16, 29, 36, 37, 43
R³	
H	1-54
C ₁₋₆ alkyl	